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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/036,819	03/09/98	SHAMI A	107-1450-C

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1641	4

DATE MAILED: 02/04/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/036,819	Applicant(s) El Shami
	Examiner S. Devi, Ph.D.	Group Art Unit 1641

☒ Responsive to communication(s) filed on *Mar 9, 1998* .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *three* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *28-40* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *28-40* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☒ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1) The instant application has been filed as a Continuation of application SN 07/303,712, filed 01/27/89, **now abandoned**, which is a Divisional application of SN 06/784,857, filed 10/04/85, **now abandoned**.

It is noted that the grand parent application, SN 06/784,857, was involved in an Interference (# 101, 933) and a judgement adverse to the Applicant was rendered.

The continuity status of applications SN 07/303,712 as disclosed in the first paragraph of the instant specification, amended through paper no. 2 filed 03/09/98, does not reflect the abandoned status as included above in bold and fails to include SN 06/784,857 as the grand parent application. Amendment to the specification is suggested to correctly reflect the continuity status.

2) Acknowledgment is made of Applicant's preliminary amendments filed 03/09/98 (paper no. 2 and 3).

With these amendments, Applicant requests the replacement of original drawings filed in the Divisional application SN 07/303,712, with the most recent formal drawings submitted in that case. Applicant further amends certain parts of the specification, cancels the original claims without referring to them by number, and adds claims 35-48, which have been renumbered as 28-40 under Rule 126.

It is noted by the Examiner of record that Applicant has **not** pointed to the specific parts of the specification that support the newly added limitations in the claims including independent and base claims.

Claims renumbered under Rule 126 as 28-40 are pending in this application and an Action on the Merits for these claims is issued in the instant Office Action.

3) Acknowledgment is made of Applicant's Declaration filed 03/09/98 along with the instant application.

Drawings

4) The drawings are objected to under 37 CFR 1.84 because of the reasons set forth by the

Draftsperson in the attached Form PTO 948 (paper no. 4). Correction is required.

Specification/Informalities

5) The specification of the instant application is objected to because:

(a) The specification contains grammatical/spelling errors: see page 27, second paragraph, line 3, for example: "tesetosterone". It is suggested that Applicant review the entire specification as this is only one example of such an error. Applicant is cautioned about the entry of new matter when amending the specification.

(b) The various Tables of the instant disclosure are illegible and the lines are improperly spaced. Legible Tables with properly spaced lines to allow easy reading and entry of amendments is required.

(c) The instant application is submitted with 20 Figures. However, the specification does not include the required section: "Brief Description of the Drawings" to describe these Figures. Further, the specification does not appear to refer to any of the submitted Figures. A reference to brief description of the drawing(s) as set forth in 37 CFR 1.74 is required.

Claim(s) Rejection(s) - 35 USC §112, Second Paragraph

6) Claims 28-40 are rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

(a) Claims 28 and 29 are vague and indefinite in the recitation "from **about** 0.246 x 10^5 up to **about** 5 x 10^5 l/mol" (emphasis added). It is unclear what is encompassed in the recitation "about" since the metes and bounds of the term are not defined in the specification.

(b) Claim 28 is confusing and incorrect in the recitation "native ligand **form** said endogenous binding proteins" (emphasis added) (see last line). Clarification/correction is required.

(c) Claims 28 and 29 are objected to because of the recitation "protein bound". The objection can be obviated by changing the recitation to --protein-bound--.

(d) Claims 28 and 29 are vague and indefinite in the recitation "significantly strip" (see

lines 9 and 10 respectively). It is not clear what is encompassed in the recitation "significantly' since the metes and bounds of the term are not defined in the specification.

(e) Claim 29 is confusing in the recitation "the concentration of free thyroxine or triiodothyronine free ligands" because it is not clear what Applicant means by "triiodothyronine free ligands". Clarification is required.

New Matter Rejection

7) Claims 28 and 29 and those dependent therefrom are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 28 and 29 currently include newly added limitations in the recitation: (ii) a specific ligand binder "at a concentration which does not significantly strip bound ligand from said endogenous proteins and having an affinity constant from about 0.246×10^5 up to about 5×10^5 l/mol". However, there appears to be no support in the instant specification for these added limitations. Applicant has **not** pointed to the specific parts of the disclosure that support the newly added limitations or amendments to the claims, and therefore the new limitations in the claims are considered to be new matter. In re Rasmussen, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See MPEP 608.04 to 608.04(c).

The Examiner of record has reviewed the Board's Decision and has noted the following: on pages 6 and 7 of the Decision, the Board states that when Applicant filed the parent Divisional application SN 07/303,712 with new claims 28-34, he indicated that "...the instant claims are directed to the use of specific ligand binders having an affinity constant of **up to about** 5×10^5 l/mol, a condition critical to obtaining accurate and true results of assays of free ligand" (emphasis added) (see page 6 of paper no. 3 of SN 07/303,712, filed 01/27/89) without pointing to the descriptive support for the newly claimed affinity constant.

It is noted by the Examiner that the current claims include an unsupported narrower range

of **affinity** constant ranging **"from about 0.246 x 10^5 up to about** 5 x 10^5 l/mol", again without pointing to the descriptive support for the now claimed range of affinity constant. A review of the instant disclosure shows the following descriptive support in the last paragraph on page 9:

> The association constant for **albumin and T4** is approximately 500,000. (This estimate is based on the assumption that the number of binding sites on the albumin molecule available for thyroxine is equal to 1, and that the apparent **association** constant in liters per mole - i.e. the equilibrium constant in the direction of complex formation - **is** 5 x 10^5 l/mol.) Likewise, the **association** constant for **albumin and T3** is approximately 24,600...." [Emphasis added].

Thus, a descriptive support does not exist in the instant specification for the specific "affinity" constant ranging from "from about 0.246 x 10^5 up to about 5 x 10^5 l/mol". The only "association" constant for albumin and T4 recited in the specification "is 5 x 10^5 l/mol". In addition, no support can be found for the recitations now added to the claims such as "affinity" constant or "a concentration which does not significantly strip bound ligand from said endogenous proteins". Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claims.

35 USC § 102

8) The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> (g) before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

35 U.S.C. § 103

9) The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person. having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 148 USPQ 459, that are applied for establishing a background for determining obviousness under 35 U.S.C. § 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or unobviousness.

Rejection Based on Public Use and Sale

10) Claims 28-40 are rejected under based upon the public use or sale of the invention, i.e. Salicylate Kits and of Immunoassay kits (see below).

The Interference 103,933 in the parent case was terminated on the grounds of prior public use.

The instant claims are unpatentable on the grounds of prior public use of products sold more than a year prior to the effective filing date of the application. See Corning Product Brochure: Single Step Free T4 [^{125}I] Radioimmunoassay, IMMO Phase, May 1984, and Corning Product Brochure: Single Step Free T4 [^{125}I] Radioimmunoassay, IMMO Phase, January 1983.

In a Declaration filed 03/09/98, Applicant discusses the issue raised by the Board about the public use of blocking agents prior to 04 October 1985, the filing date of the grand parent application 784,857, the application that was involved in the Interference. Applicant contends that the Diagnostic Products Corporation (DPC) to which the instant application is assigned to:

> ...first began the use of blocking agents in analog based assays for free hormones in 1982. The first product, which was released on July 15, 1982, contained 0.5% salicylate at 1x concentration as a selective blocker for albumin in a Free T4 assay. Free T3 assay was released on February 4, 1983 and also contained sodium salicylate as the selective blocker for albumin. However, these products and all other products released prior to October 4, 1984 did not contain an antibody (ligand binder) that was of an affinity and at a concentration effective to avoid stripping of T3 and T4 off of endogenous proteins.

Applicant's statement regarding the absence of antibody as ligand binder in kits sold prior to October 4, 1984 is not viewed to be non-persuasive because, as noted by the Board, there is no descriptive support in the instant disclosure for an "antibody (ligand binder)" with the recited range of affinity constant and a concentration effective to avoid stripping of T3 and T4 off of

endogenous proteins (see paragraph 7 above) and the now recited numerical range of affinity constant is not asserted to be critical for the invention. The only "association" constant disclosed is for albumin and T4 which is recited as "5 x 10^5 l/mol" (see page 9 of the disclosure).

Rejection Based on the Lost Interference Count

11) In accordance with the practice set out in MPEP 2363, claims 28-40 are rejected under 35 U.S.C. § 103 as being unpatentable over the count of Interference no. 101,933.

The count 1 of Interference no. 101,933 is provided below:

> In a method of determining the concentration of a free portion of a ligand in a biological fluid, wherein said free ligand is in equilibrium with another portion of the ligand bound to one or more endogenous binders in said fluid comprising the steps of (a) forming a mixture of a sample of said fluid with (1) an amount of a specific binder for the free ligand insufficient to substantially affect said equilibrium, and (2) a labeled derivative of the ligand that binds to said specific binder and has affinity for the endogenous binders lower than that of the ligand for said endogenous binders, (b) maintained said mixture to permit the ligand derivative to complete with the free ligand for binding with the specific binder, (c) measuring the amount of ligand derivative that has, or has not, become bound to the specific binder, and (d) determining the concentration of said free ligand from said measurement, wherein the improvement comprises including in the mixture an amount of a blocking agent which substantially reduces the binding of the ligand derivative to the endogenous binders without substantially reducing the binding of the ligand to said endogenous binders.

The count clearly embraces the use of a specific binding ligand with any affinity. Applicant has now included a narrower range of affinity constant ranging "from about 0.246 x 10^5 up to about 5 x 10^5 l/mol". However, since no evidence is of record in the instant disclosure establishing that the now claimed numerical limitation is critical for the invention and/or the now claimed range provides any unexpected results, the claims are unpatentable or obvious over the count.

It is noted that a similar rejection made in the parent case SN 07/303,712 was affirmed by the Board. In that parent case, the base claim recited "an affinity constant up to least about 5 x 10^5 l/mol". The Board's position was that since there is generic reference in the count to specific binding ligand which ligand can be of any affinity, the count is suggestive of the subgenus now claimed. Since the now added numerical limitation of "from about 0.246 x 10^5 up to about 5 x 10^5 l/mol" would likewise be subgeneric to the count, the instant claims are rejected over the count of Interference no. 103,933.

Remarks

12) No claims are allowed.

13) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 8.00 am to 4.00 pm. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, James Housel, can be reached on (703) 308-4027. The fax phone number for this Group is (703) 305-7939.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

January 1999

James C. Housel
JAMES C. HOUSEL 2/1/99
SUPERVISORY PATENT EXAMINER